Office Action Summary	Application No.	Applicant(s)	
	10/650,608	CASSART ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *8/5/08 and 10/14/08*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) _____ is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/14/08;1/11/08*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *9/9/08* .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 7-9 are examined in the instant application.

Claim Rejections - 35 USC § 112, First Paragraph, Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7-9 remain rejected under 35 U.S.C. 112, first paragraph, because the specification and the claims lack enablement for a method for inducing an immune response to SEQ ID NO:2 in a human, or non-human animal, using a peptide fragment of SEQ ID NO:2, comprising SEQ ID NO:25, for reasons already of record in paper of 03/05/08.

The response asserts as follows: The rejection should be withdrawn for two (2) main reasons. (1) The Office's claim construction is legally incorrect; and (2) the rejection is founded on statements of fact that are either conclusory or contradicted by the evidence of record.

Reason (1): Incorrect Claims Construction. The rejection miss-construes the claims as if they recite an endpoint of tumor reduction. Applicants have brought this erroneous construction to the attention of the Office without avail. None of the claims group currently under examination by the Office ever recited "treating cancer," "cancer treatment," "tumor reduction," or the like, nor do any of the currently pending claims recite "treating cancer," "cancer treatment," "tumor reduction," or the like. Essentially, the Office is improperly reading a tumor reduction limitation into the claims. The Office is not utilizing the specification to interpret a

term or clause in the claims. Rather, it is reading a limitation into the claims from text found in the specification. Moreover, the cited portion of the specification is the Examples section. One of the Examples does relate to experiments that can be carried out to identify T-cells that specifically react to the polypeptide of SEQ ID NO:2. But there is no basis in patent law to read subject matter from the examples into a claim, as has been done here. (It is worth noting that one of the other examples--Example 10--actually discloses the induction of an immune response to a peptide comprising SEQ ID NO:25.) Due to of the Office's erroneous claim construction, the remainder of the rejection is ill-founded because it does not relate to whether Applicants have enabled methods of inducing an immunoresponse. Applicants maintain that their methods are enabled. Supporting data can be found in the Examples (see, e.g., Example 10, in which a cell mediated response to the peptide recited in claim 7 is demonstrated; see also, Examples 12 and 17, which demonstrates that other disclosed peptides also induce an immune response, namely a specific antibody response in rabbits). The rejection of claims 7-9 should be withdrawn because it is based upon an incorrect claim construction.

The response has been considered but is not found to be persuasive for the following reasons:

Rejection remains for the following main reasons: (1) The Office's claim interpretation is legally correct (See ln re Van Geuns. 988 F.2d 1181, 26 USPQZd 1057 (Fed. Cir. 1993); and (2) The rejection is based the teaching in the art, which overwhelming indicates that cancer immunotherapy is highly unpredictable. Further, there is no evidence that cited art contradicts with the reference submitted in the response.

The specification contemplates the use of the claimed polypeptide for diagnosis or treatment of cancer throughout the specification (see for example, p.1, lines 17-21, Summary on p.2, lines 6-18, p.26, line 25, p.43, line 29), including contemplating testing the effect of the stimulated T cells on tumor cells transfected with cDNA encoding SEQ ID NO:2 (p.64, last two paragraphs, bridging p.65). In light of the specification, the claims are **reasonably interpreted** as a method for **treating cancer**, such as reduction of cancer cell growth in vivo, or a method for **inducing an immune response in** a human or non-human animal having **cancer**. Example 10, p.68-71, in the specification, discloses an **in vitro** method of inducing a CTL immune response of a fragment of SEQ ID NO:2, i.e., the peptide SEQ ID NO:25, which is not applicable to the claimed in vivo method, and Examples 12, 17, p.72, and p. 82-87, disclose that the disclosed peptides induce antibody production in rabbits, or mice, which rabbits or mice **do not have cancer**. The **limitation of Examples 12, 17** disclosed in the specification, i.e., **inducing an antibody in an animal that does not have cancer**, certainly would not be used to limit the claims in claim interpretation.

Although the claims are interpreted in light of the specification, **limitations from the specification are not read into the claims** (emphasis added)**.** See ln re Van Geuns. 988 F.2d 1181, 26 USPQZd 1057 (Fed. Cir. 1993).

The response further asserts as follows:

Reason (2): Concerning the cited references by Kirkin, Boone, Gaiger, Ezzell, and Spitler, Applicants submitted a reference that rebuts Gaiger. (See the Response, dated 18 Jul 07, discussing Oka et al. which demonstrates that WT-1 peptides are immunogenic and effective in

vivo.). The rest of these references are irrelevant because of their age: Kirkin, Boone, Ezzell, and Spitler were published in the 1990s.

Concerning Smith, Boone, and White, which discuss immunosuppression and immune tolerance in cancer, Smith and Boone are mainly of interest in a historical sense, dating from 1994 and 1992, respectively. White does not relate to the cancer antigen of Applicants' disclosure, namely CASB7439/ASCL2/HASH2, and White is therefore irrelevant to whether CASB7439/ASCL2/HASH2 would be internalized in a cancer cell. Nonetheless, the Office has continued to rely on White, stating "one cannot predict the behavior of an antigen unless tested." But Applicants have tested their antigen and the evidence of record favors a conclusion that ASCL2/HASH2 protein (i) is over-expressed on cancer cells, not normal cells, and (ii) is not internalized. See Example 11, which demonstrates by immunohistochemistry that CASB7439/ASCL2/HASH2 staining is high in colon cancer and low in normal colon. These results favor a conclusion that CASB7439/ASCL2/HASH2 protein is present on the surface of colon cancer cells (because it is accessible to staining).

The response has been considered but is not found to be persuasive for the following reasons:

Although the references by Kirkin, Boone, Gaiger, Ezzell, and Spitler are published in the 1990, there is no evidence that their teaching does not apply to the claimed invention, and the present state of the art. This is evidenced by the confirmation of their teaching by Bodey et al, 2000, Anticancer Res, 20: 2665-2676. Bodey et al confirm the teaching of Boon and Smith, by explaining the reasons for failure of vaccine in human. Bodey et al teach that although general immune activation against the target antigens has been documented in most cases, reduction of

tumor load has not been frequently observed in human patients (abstract, second column, p.2673). Bodey et al teach that the failure of cancer vaccine is due to natural selection of highly aggressive clones in the treated patient, said clones no longer express the cancer specific antigen (abstract, second column, p.2673). Bodey et al teach that these clones of tumor cells survive the immune system, through secretion of immunoinhibitory cytokines, downregulation of MHC, loss of costimulatory molecules, and induction of T cell anergy (p.2673, second column, last paragraph). In addition, Mellman I, 2006, The Scientist, 20(1): 47-56, teaches that immunotherapy of cancer has yet to live up to expectations (p.47). Mellmann teaches that attempts at using cytokines to stimulate anticancer T cells, or deploying toxin-conjugated antibodies as magic bullets were never quite successful, and that therapeutic vaccines for cancer have proven similarly disappointing (p.47). Furthermore, Kaiser (Science, 2006, 313, 1370) teaches that 90% of tumor drugs fail in patients, see 3rd col., 2nd to last para.

Concerning Gaiger and Oka, the references do not contradict each other, because the WT-1 peptide taught by Gaiger et al is different from that taught the teaching of Oka (previous Office action, p.7, third paragraph). Although the WT-1 peptide taught by Oka et al is effective in inducing cancer regression, the WT-1 peptide taught by Geiger et al, which although show in vivo CTL response, but is not effective in treating cancer, is different from that taught the teaching of Oka (previous Office action, p.7, third paragraph). Further, although inducing CTL response in vivo, the WT-1 peptide taught by Gaiger et al does not have any effect on cancer growth in vivo, thus demonstrating that even the ability to inducing a CTL response in vivo does not necessarily lead to any result of any practical use. Thus, based on the teaching of Gaiger and

Oka, one cannot predict which of the peptides of a full length protein is effective in treating cancer.

Further, although the references by Smith and Boone are published in the 1990, there is no evidence that their teaching of iimunosuppression and immune tolerance does not apply to the claimed invention, and the present state of the art. This is evidenced by the confirmation of their teaching by Bodey et al, 2000, supra. Bodey et al teach that these clones of tumor cells survive the immune system, through secretion of immunoinhibitory cytokines, downregulation of MHC, loss of costimulatory molecules, and induction of T cell anergy (p.2673, second column, last paragraph).

In addition, in view of the teaching of White et al, one cannot predict whether the claimed antigen is not internalized or downregulated in cancer cells and is of sufficient quantity on the cancer cell surface, such that it can be recognized by specific antibody or CTLs, necessarily for cancer treatment. Further, as stated by Applicant in the interview of 10/14/08, due to property of immunohistochemistry, antigen detection by immunohistochemistry in Example 11 does not show that the claimed peptide is not internalized, and is of sufficient quantity on the cancer cell surface, such that it can be recognized by specific antibody or CTLs, necessarily for cancer treatment.

The response further asserts that even if the claims under examination were drawn to methods of treating cancer, the Office's requirement of a successful cancer therapeutic would be an inappropriately high standard for enablement. See In re Brana, 51 F.3d 1560, 1566, 34

USPQ2d 1436, 1441 (Fed. Cir. 1995)(requiring information of the sort necessary for regulatory approval not an appropriate standard by which to judge patentability).

The response has been considered but is not found to be persuasive for the following reasons:

The requirement of a successful cancer therapeutic is not high standard for enablement, because all it requires is an in vivo reduction of cancer cell growth, and does not require clinical trial.

The response further asserts as follows:

Miscellaneous. Applicants have pointed out that the Office's improper claim construction harms Applicants because by limiting the claims to therapeutic methods, the Office fails to consider other bona fide uses for Applicants' claimed methods for inducing an immunoresponse. Applicants have disclosed that their methods can be used "to generate antibodies or reagents specific for the polypeptide of the present invention, as diagnostic reagents to detect...genetic or biochemical markers in blood or tissues that will enable the detection of very early changes along the carcinogenesis pathway will help in determining the best treatment for the patient." See US20050260634, paragraphs [0182]-[183].

The Office's response that "Applicants argue limitation[s] not in the claim. The claims are not drawn to a method for diagnosis of cancer, by inducing an immune response" appears to take the position that the use need not be considered unless it is expressly recited in the claim, but there is no support for such a proposition. Indeed, it is a well-understood tenant of patent law that the claims themselves need not recite any utility (only the specification must describe a utility).

Thus, the Office's failure to consider the utility described above cannot be supported and the rejection of claims 7-9 should be withdrawn for this reason, as well.

The response has been considered but is not found to be persuasive for the following reasons:

Although the specific method for making an antibody in a non-cancerous subject is enabled, however, the claimed method is broad, and is not enable, because it encompasses a method for making an antibody or CTLs in a subject burdened with cancer, or a method for treating cancer, for reasons set forth above, and in previous Office action. Further, the claimed method also ecompasses a method for making an antibody in a healthy human. However, different from a healthy non-human animal, one would not use a healthy human to produce an antibody for its commercial application.

The response asserts as follows:

Claim 9. There is no reason for the Office to require a showing of synergy and no basis in the Rules has been cited for this requirement.

The response has been considered but is not found to be persuasive for the following reasons:

Without a demonstrated synergy effect of the adjuvant, i.e., an effect other than an additive effect of the adjuvant, the claimed method is not enabled, because the claimed peptide per se is not enabled for treatment of cancer, or inducing a sufficient amount of antibody or CTLs in a cancer patient, necessary for reducing cancer cell growth. Although some adjuvant is known to be able to induce a reduction in cancer cell growth, the result of a claimed method,

when based solely on the property of another compound known in the art, such as a known adjuvant, is not innovative and therefore, is not allowable.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, LARRY HELMS can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MINH TAM DAVIS
November 21, 2008

/Larry R. Helms/

Supervisory Patent Examiner, Art Unit 1643